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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/652,345	08/31/2000	David H. Farb	0146-2026	2909

7590 06/10/2002
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EXAMINER

LI, RUIXIANG

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 06/10/2002

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/652,345

Applicant(s)

FARB ET AL.

Examiner

Ruixiang Li

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-29 and 32-65 is/are pending in the application.
- 4a) Of the above claim(s) 12-25 and 34-57 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11, 26-29, 32, 33 and 58-65 is/are rejected.
- 7) ☒ Claim(s) 10 is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08/31/2000 is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 16.
- 18) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____.

DETAILED ACTION

I. Election/Restrictions

Applicants' affirmation of the election of species A (NMDA receptors with identical NR2 subunits and different NR1 subunits) within Group I, in Paper No. 18 is acknowledged.

II. Status of Application, Amendments, and/or Claims

The amendment filed in Paper No. 18 on May 5, 2002 has been entered in full. Claims 30 and 31 have been canceled. Claims 1 and 2 have been amended. Claims 58-65 have been added. Claims 1-29 and 32-65 remain pending. Claims 1-11, 26-29, 32, 33, and 58-65 are under consideration. Claims 12-25 and 34-57 are withdrawn from further consideration because they are drawn to unelected subject matter.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

III. Withdrawn Objections and/or Rejections

The objection to the specification, as set forth at pages 2-3 of the previous Office Action (Paper No. 14, December 3, 2001), has been withdrawn in view of applicants' amendment.

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The rejection of Claim 2 under 35 U.S.C. 112, 2nd paragraph, as set forth at page 3 of the previous Office Action (Paper No. 14, December 3, 2001), has been withdrawn in view of applicants' amendment of Claim 2.

The rejection of Claims 1, 2, and 26-33 under 35 U.S.C. 102 (b), as set forth at page 4 (item No. 9) of the previous Office Action (Paper No. 14, December 3, 2001), has been withdrawn in view of applicants' amendment of Claim 1.

The rejection of Claims 1, 2, 26-29, and 31-33 under 35 U.S.C. 102 (b), as set forth at pages 4-5 (item No. 10) of the previous Office Action (Paper No. 14, December 3, 2001), has been withdrawn in view of applicants' amendment of Claim 1.

The rejection of Claims 1-6, 26-28, 31, and 33 under 35 U.S.C. 102 (b), as set forth at page 5 (item No. 11) of the previous Office Action (Paper No. 14, December 3, 2001), has been withdrawn in view of applicants' amendment of Claim 1.

The rejection of Claims 1-5, 7, 26-29, and 31 under 35 U.S.C. 102 (b), as set forth at pages 5-6 (item No. 12) of the previous Office Action (Paper No. 14, December 3, 2001), has been withdrawn in view of applicants' amendment of Claim 1.

The rejection of Claims 1-5, 8, 26-29, 31, and 33 under 35 U.S.C. 102 (b), as set forth at page 6 (item No. 13) of the previous Office Action (Paper No. 14, December 3, 2001), has been withdrawn in view of applicants' amendment of Claim 1.

The rejection of Claims 1-6, 8, 11, 26-28, 31, and 33 under 35 U.S.C. 102 (b), as set forth at page 6 (item No. 14) of the previous Office Action (Paper No. 14, December 3, 2001), has been withdrawn in view of applicants' amendment of Claim 1.

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The rejection of Claim 9 under 35 U.S.C. 103 (a), as set forth at pages 7-8 (item No. 16) of the previous Office Action (Paper No. 14, December 3, 2001), has been withdrawn in view of applicants' amendment of Claim 1, upon which Claim 9 depends.

IV. Objections to Drawings

The proposed drawing correction of Figure 1 has been approved by the examiner. A proper drawing correction of Figure 1 and other figures are required in reply to the Office action to avoid abandonment of the application. The correction to the drawings will not be held in abeyance.

V. Claim Rejections Under 35 U. S. C. § 112, 2nd Paragraph

Claim 59 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 59 recites the limitation "the subset of the NMDA receptors" in the 2nd line of Claim 59. There is insufficient antecedent basis for this limitation in the claim.

VI. Claim Rejections—35 USC § 103

Claims 1-9, 11, 26-29, 32, 33, 58-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park-Chung et al. (IDS, Paper # 7, *Mol. Pharmacol.* 52 :1113-1123, 1997) in view of Williams et al. (*Mol. Pharmacol.* 45:803-809, 1994), Daggett et al (U.S. Patent number 5,849,895, 12/15/1998), Masuko et al. (*Mol. Pharmacol.* 55:957-969, June 1999), Traynelis et al. (*J. Neurosci.* 18:6163-6175, 1998).

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Park-Chung et al. teach a method of identifying subunit specific steroid modulators of the N-methyl-D-aspartate (NMDA) receptor in *Xenopus laevis* oocytes expressing NR1₁₀₀ and NR2A subunits (see, in particular, page 1119, 2nd paragraph of left hand column). Chung et al. also teach that the response of NMDA receptor to agonists (NMDA, glutamate, and glycine) or antagonist (APV, D-2-amino-5-phosphonovaleric acid; Fig. 7 and page 1119, 3rd paragraph of left hand column) were modulated by steroid modulators (e.g., pregnenolone sulfate and 3 β 5 β S (3 β -hydroxy-5 β -pregnan-20-one sulfate). Further, Park-Chung et al. teach the use of non-steroid modulators (page 1113)—small molecules: polyamine, e.g., spermine (page 1116, Fig. 3); redox, e.g., DTT (Fig. 5); and arachidonic acid (Fig. 4, page 1117).

Chung et al. fail to teach “providing a plurality of recombinant NMDA receptors which differ in their subunit identity” and NMDA receptors with various mutations.

However, Williams et al. teach the characterization of differential modulatory effects of spermine on NMDA receptors with identical NR2 subunits and different NR1 subunits expressed in oocytes, including NR1A/NR2A and NR1B/NR2A (Fig. 1). Please note that NR1A is NR1₀₁₁ whereas NR1B is NR1₁₁₁. NR1B contains an α exon.

Daggett et al. teach NMDA receptor subunits, homomeric and heteromeric NMDA receptors comprising these subunits (column 15, 2nd paragraph). Daggett et al also teach NMDA receptors with identical NR2 subunits and different NR1 subunits expressed in oocytes (Table 1), chimeric isoforms of NMDAR1A, for example, NMDAR1-I63-delta-363 (See example 2, section D). Please note that NMDAR1A is NR1₀₁₁.

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Masuko et al. teach various mutations in the NR1 subunit (NR1A or NR011) of NR1/NR2B receptors expressed in *Xenopus*, including point mutations at NR1A subunit include point mutations at a residue at 181, 192, 198, 227, 251 or 253 (See Fig. 2).

Traynelis et al. teach differential responses of point mutants of NR1 subunits (NR1a and NR1b) of various NR1/NR2 receptors expressed in *Xenopus oocytes* to glutamate and glycine modulated by spermine and zinc (see, in particular, Fig. 3). Please note that point mutants of NR1b contain an α exon.

Therefore, It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the methods of Park-Chung et al. so as to include additional recombinant NMDA receptors taught by Williams et al., and NMDA receptors with various mutations taught by Williams et al., Daggett et al., Masuko et al. and Traynelis et al. with a reasonable expectation of success. The motivation to do so would have been in the recognition that determination of the effect of the drug substances on specific receptor subunits or mutations should permit development and screening receptor subtype-specific or disease-specific drugs and reduction of unwanted side effects, as suggested by Daggett et al. (U.S. Patent number 5,849,895, 12/15/1998, column 15, 4th and 5th paragraphs) and the expression of recombinant NMDA receptors in, e.g., *Xenopus oocytes*, provides an ideal approach to examine the biological functions of the NMDA receptors and to evaluate the effect of modulators on the NMDA receptors, as demonstrated by Park-Chung et al., Williams et al., Daggett et al., Masuko et al. and Traynelis et al.

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VII. Claim Objection

Claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

VIII. Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday-Friday, 8:30 am-5:00 pm.

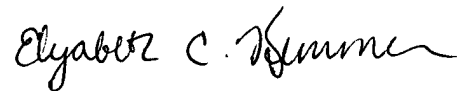
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Ruixiang Li
Examiner
June 5, 2002

ELIZABETH KEMMERER
PRIMARY EXAMINER